○ 280   OIPE

Serial Number: **10/001,844**

ENTERED

CRF Processing Date: **12/11/2001**
Edited by: _____
Verified by: _____ (STIC sta[

#2

☐ Changed a file from non-ASCII to ASCII

☐ Changed the margins in cases where the sequence text was "wrapped" down to the next line

☐ Edited a format error in the Current Application Data section, specifically:
_____

☐ Edited the Current Application Data section with the actual current number. The number inputted by the applicant was ☐ the prior application data; or ☐ other _____

☐ Added the mandatory heading and subheadings for "Current Application Data".

☐ Edited the "Number of Sequences" field. The applicant spelled out a number instead of using an integer.

☐ Changed the spelling of a mandatory field (the headings or subheadings), specifically:
_____

☐ Corrected the SEQ ID NO when obviously incorrect. The sequence numbers that were edited were:
_____

☐ Inserted or corrected a nucleic number at the end of a nucleic line. SEQ ID NO's edited:
_____

☐ Corrected subheading placement. All responses must be on the same line as each subheading. If the applicant placed a response below the subheading, this was moved to its appropriate place.

☐ Inserted colons after headings/subheadings. Headings edited included: . .
_____

☐ Deleted extra, invalid, headings used by an applicant, specifically:
_____

☑ Deleted: ☑ non-ASCII "garbage" at the beginning/end of files; ☐ secretary initials/filename at end of file; ☐ page numbers throughout text; ☐ other invalid text, such as _____

☐ Inserted mandatory headings, specifically: _____

☐ Corrected an obvious error in the response, specifically:
_____

☐ Edited identifiers where upper case is used but lower case is required, or vice versa.

☐ Corrected an error in the Number of Sequences field, specifically:
_____

☐ A "Hard Page Break" code was inserted by the applicant. All occurrences had to be deleted.

☐ Deleted ending stop codon in amino acid sequences and adjusted the "(A)Length:" field accordingly (error due to a PatentIn bug). Sequences corrected: _____

☐ Other:
_____
_____
_____

Examiner: The above corrections must be communicated to the applicant in the first Office Action. DO NOT send a copy of this form.

3/1/95

#2

OIPE

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/001,844

DATE: 12/11/2001
TIME: 20:33:03

Input Set : A:\Pto.amc
Output Set: N:\CRF3\12112001\I001844.raw

```
   4 <110> APPLICANT: C. Frank Bennett
   5        Lex M. Cowsert
   7 <120> TITLE OF INVENTION: ANTISENSE MODULATION OF SHH EXPRESSION
   9 <130> FILE REFERENCE: ISPH-0617
C--> 11 <140> CURRENT APPLICATION NUMBER: US/10/001,844
C--> 11 <141> CURRENT FILING DATE: 2001-11-16
  11 <160> NUMBER OF SEQ ID NOS: 49
  13 <170> SOFTWARE: FastSEQ for Windows Version 4.0
  15 <210> SEQ ID NO: 1
  16 <211> LENGTH: 20
  17 <212> TYPE: DNA
  18 <213> ORGANISM: Artificial Sequence
  20 <220> FEATURE:
  21 <223> OTHER INFORMATION: Antisense Oligonucleotide
  23 <400> SEQUENCE: 1
  24 tccgtcatcg ctcctcaggg                                        20
  26 <210> SEQ ID NO: 2
  27 <211> LENGTH: 20
  28 <212> TYPE: DNA
  29 <213> ORGANISM: Artificial Sequence
  31 <220> FEATURE:
  32 <223> OTHER INFORMATION: Antisense Oligonucleotide
  34 <400> SEQUENCE: 2
  35 atgcattctg cccccaagga                                        20
  37 <210> SEQ ID NO: 3
  38 <211> LENGTH: 1576
  39 <212> TYPE: DNA
  40 <213> ORGANISM: Homo sapiens
  42 <220> FEATURE:
  43 <221> NAME/KEY: CDS
  44 <222> LOCATION: (152)...(1540)
  46 <400> SEQUENCE: 3
  47 gcgaggcagc cagcgaggga gagagcgagc gggcgagccg gagcgaggaa gggaaagcgc 60
  48 aagagagagc gcacacgcac acacccgccg cgcgcactcg cgcccggacc cgcacgggga 120
  49 cagctcggaa gtcatcagtt ccatgggcga g atg ctg ctg ctg gcg aga tgt  172
  50                                    Met Leu Leu Leu Ala Arg Cys
  51                                     1               5
  53 ctg ctg cta gtc ctc gtc tcc tcg ctg ctg gta tgc tcg gga ctg gcg  220
  54 Leu Leu Leu Val Leu Val Ser Ser Leu Leu Val Cys Ser Gly Leu Ala
  55          10                  15                  20
  57 tgc gga ccg ggc agg ggg ttc ggg aag agg agg cac ccc aaa aag ctg  268
  58 Cys Gly Pro Gly Arg Gly Phe Gly Lys Arg Arg His Pro Lys Lys Leu
  59          25                  30                  35
  61 acc cct tta gcc tac aag cag ttt atc ccc aat gtg gcc gag aag acc  316
  62 Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
  63   40                  45                  50                  55
  65 cta ggc gcc agc gga agg tat gaa ggg aag atc tcc aga aac tcc gag  364
```

```
66 Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Ser Arg Asn Ser Glu
67                 60              65                  70
69 cga ttt aag gaa ctc acc ccc aat tac aac ccc gac atc ata ttt aag    412
70 Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys
71             75              80                  85
73 gat gaa gaa aac acc gga gcg gac agg ctg atg act cag agg tgt aag    460
74 Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys
75             90              95                 100
77 gac aag ttg aac gct ttg gcc atc tcg gtg atg aac cag tgg cca gga    508
78 Asp Lys Leu Asn Ala Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly
79         105             110                 115
81 gtg aaa ctg cgg gtg acc gag ggc tgg gac gaa gat ggc cac cac tca    556
82 Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser
83 120             125             130                 135
85 gag gag tct ctg cac tac gag ggc cgc gca gtg gac atc acc acg tct    604
86 Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser
87             140             145                 150
89 gac cgc gac cgc agc aag tac ggc atg ctg gcc cgc ctg gcg gtg gag    652
90 Asp Arg Asp Arg Ser Lys Tyr Gly Met Leu Ala Arg Leu Ala Val Glu
91             155             160                 165
93 gcc ggc ttc gac tgg gtg tac tac gag tcc aag gca cat atc cac tgc    700
94 Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys
95             170             175                 180
97 tcg gtg aaa gca gag aac tcg gtg gcg gcc aaa tcg gga ggc tgc ttc    748
98 Ser Val Lys Ala Glu Asn Ser Val Ala Ala Lys Ser Gly Gly Cys Phe
99         185             190             195
101 ccg ggc tcg gcc acg gtg cac ctg gag cag ggc ggc acc aag ctg gtg   796
102 Pro Gly Ser Ala Thr Val His Leu Glu Gln Gly Gly Thr Lys Leu Val
103 200             205             210                 215
105 aag gac ctg agc ccc ggg gac cgc gtg ctg gcg gcg gac gac cag ggc   844
106 Lys Asp Leu Ser Pro Gly Asp Arg Val Leu Ala Ala Asp Asp Gln Gly
107             220             225                 230
109 cgg ctg ctc tac agc gac ttc ctc act ttc ctg gac cgc gac gac ggc   892
110 Arg Leu Leu Tyr Ser Asp Phe Leu Thr Phe Leu Asp Arg Asp Asp Gly
111             235             240                 245
113 gcc aag aag gtc ttc tac gtg atc gag acg cgg gag ccg cgc gag cgc   940
114 Ala Lys Lys Val Phe Tyr Val Ile Glu Thr Arg Glu Pro Arg Glu Arg
115             250             255                 260
117 ctg ctg ctc acc gcc gcg cac ctg ctc ttt gtg gcg ccg cac aac gac   988
118 Leu Leu Leu Thr Ala Ala His Leu Leu Phe Val Ala Pro His Asn Asp
119         265             270             275
121 tcg gcc acc ggg gag ccc gag gcg tcc tcg ggc tcg ggg ccg cct tcc  1036
122 Ser Ala Thr Gly Glu Pro Glu Ala Ser Ser Gly Ser Gly Pro Pro Ser
123 280             285             290                 295
125 ggg ggc gca ctg ggg cct cgg gcg ctg ttc gcc agc cgc gtg cgc ccg  1084
126 Gly Gly Ala Leu Gly Pro Arg Ala Leu Phe Ala Ser Arg Val Arg Pro
127             300             305                 310
129 ggc cag cgc gtg tac gtg gtg gcc gag cgt gac ggg gac cgc cgg ctc  1132
130 Gly Gln Arg Val Tyr Val Val Ala Glu Arg Asp Gly Asp Arg Arg Leu
```

```
131              315                 320                 325
133 ctg ccc gcc gct gtg cac agc gtg acc cta agc gag gag gcc gcg ggc   1180
134 Leu Pro Ala Ala Val His Ser Val Thr Leu Ser Glu Glu Ala Ala Gly
135         330                 335                 340
137 gcc tac gcg ccg ctc acg gcc cag ggc acc att ctc atc aac cgg gtg   1228
138 Ala Tyr Ala Pro Leu Thr Ala Gln Gly Thr Ile Leu Ile Asn Arg Val
139         345                 350                 355
141 ctg gcc tcg tgc tac gcg gtc atc gag gag cac agc tgg gcg cac cgg   1276
142 Leu Ala Ser Cys Tyr Ala Val Ile Glu Glu His Ser Trp Ala His Arg
143 360                 365                 370                 375
145 gcc ttc gcg ccc ttc cgc ctg gcg cac gcg ctc ctg gct gca ctg gcg   1324
146 Ala Phe Ala Pro Phe Arg Leu Ala His Ala Leu Leu Ala Ala Leu Ala
147         380                 385                 390
149 ccc gcg cgc acg gac cgc ggc ggg gac agc ggc ggc ggg gac cgc ggg   1372
150 Pro Ala Arg Thr Asp Arg Gly Gly Asp Ser Gly Gly Gly Asp Arg Gly
151         395                 400                 405
153 ggc ggc ggc ggc aga gta gcc cta acc gct cca ggt gct gcc gac gct   1420
154 Gly Gly Gly Gly Arg Val Ala Leu Thr Ala Pro Gly Ala Ala Asp Ala
155         410                 415                 420
157 ccg ggt gcg ggg gcc acc gcg ggc atc cac tgg tac tcg cag ctg ctc   1468
158 Pro Gly Ala Gly Ala Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu
159     425                 430                 435
161 tac caa ata ggc acc tgg ctc ctg gac agc gag gcc ctg cac ccg ctg   1516
162 Tyr Gln Ile Gly Thr Trp Leu Leu Asp Ser Glu Ala Leu His Pro Leu
163 440                 445                 450                 455
165 ggc atg gcg gtc aag tcc agc tga agccgggggg ccgggggagg ggcgcgggag   1570
166 Gly Met Ala Val Lys Ser Ser  *
167                 460
169 ggggcc                                                             1576
```

171 <210> SEQ ID NO: 4
172 <211> LENGTH: 21
173 <212> TYPE: DNA
174 <213> ORGANISM: Artificial Sequence
176 <220> FEATURE:
177 <223> OTHER INFORMATION: PCR Primer
179 <400> SEQUENCE: 4
180 cggcttcgac tgggtgtact a   21
182 <210> SEQ ID NO: 5
183 <211> LENGTH: 17
184 <212> TYPE: DNA
185 <213> ORGANISM: Artificial Sequence
187 <220> FEATURE:
188 <223> OTHER INFORMATION: PCR Primer
190 <400> SEQUENCE: 5
191 gcagcctccc gatttgg   17
193 <210> SEQ ID NO: 6
194 <211> LENGTH: 30
195 <212> TYPE: DNA
196 <213> ORGANISM: Artificial Sequence

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/001,844

DATE: 12/11/2001
TIME: 20:33:03

Input Set : **A:\Pto.amc**
Output Set: **N:\CRF3\12112001\I001844.raw**

```
198 <220> FEATURE:
199 <223> OTHER INFORMATION: PCR Probe
201 <400> SEQUENCE: 6
202 tatccactgc tcggtgaaag cagagaactc                    30
204 <210> SEQ ID NO: 7
205 <211> LENGTH: 19
206 <212> TYPE: DNA
207 <213> ORGANISM: Artificial Sequence
209 <220> FEATURE:
210 <223> OTHER INFORMATION: PCR Primer
212 <400> SEQUENCE: 7
213 gaaggtgaag gtcggagtc                                19
215 <210> SEQ ID NO: 8
216 <211> LENGTH: 20
217 <212> TYPE: DNA
218 <213> ORGANISM: Artificial Sequence
220 <220> FEATURE:
221 <223> OTHER INFORMATION: PCR Primer
223 <400> SEQUENCE: 8
224 gaagatggtg atgggatttc                               20
226 <210> SEQ ID NO: 9
227 <211> LENGTH: 20
228 <212> TYPE: DNA
229 <213> ORGANISM: Artificial Sequence
231 <220> FEATURE:
232 <223> OTHER INFORMATION: PCR Probe
234 <400> SEQUENCE: 9
235 caagcttccc gttctcagcc                               20
237 <210> SEQ ID NO: 10
238 <211> LENGTH: 20
239 <212> TYPE: DNA
240 <213> ORGANISM: Artificial Sequence
242 <220> FEATURE:
243 <223> OTHER INFORMATION: Antisense Oligonucleotide
245 <400> SEQUENCE: 10
246 gcccgctcgc tctctccctc                               20
248 <210> SEQ ID NO: 11
249 <211> LENGTH: 20
250 <212> TYPE: DNA
251 <213> ORGANISM: Artificial Sequence
253 <220> FEATURE:
254 <223> OTHER INFORMATION: Antisense Oligonucleotide
256 <400> SEQUENCE: 11
257 ggcgggtgtg tgcgtgtgcg                               20
259 <210> SEQ ID NO: 12
260 <211> LENGTH: 20
261 <212> TYPE: DNA
262 <213> ORGANISM: Artificial Sequence
264 <220> FEATURE:
```

```
265 <223> OTHER INFORMATION: Antisense Oligonucleotide
267 <400> SEQUENCE: 12
268 ccgtgcgggt ccgggcgcga                                    20
270 <210> SEQ ID NO: 13
271 <211> LENGTH: 20
272 <212> TYPE: DNA
273 <213> ORGANISM: Artificial Sequence
275 <220> FEATURE:
276 <223> OTHER INFORMATION: Antisense Oligonucleotide
278 <400> SEQUENCE: 13
279 tctcgcccat ggaactgatg                                    20
281 <210> SEQ ID NO: 14
282 <211> LENGTH: 20
283 <212> TYPE: DNA
284 <213> ORGANISM: Artificial Sequence
286 <220> FEATURE:
287 <223> OTHER INFORMATION: Antisense Oligonucleotide
289 <400> SEQUENCE: 14
290 catctcgccc atggaactga                                    20
292 <210> SEQ ID NO: 15
293 <211> LENGTH: 20
294 <212> TYPE: DNA
295 <213> ORGANISM: Artificial Sequence
297 <220> FEATURE:
298 <223> OTHER INFORMATION: Antisense Oligonucleotide
300 <400> SEQUENCE: 15
301 agcatctcgc ccatggaact                                    20
303 <210> SEQ ID NO: 16
304 <211> LENGTH: 20
305 <212> TYPE: DNA
306 <213> ORGANISM: Artificial Sequence
308 <220> FEATURE:
309 <223> OTHER INFORMATION: Antisense Oligonucleotide
311 <400> SEQUENCE: 16
312 gcagcatctc gcccatggaa                                    20
314 <210> SEQ ID NO: 17
315 <211> LENGTH: 20
316 <212> TYPE: DNA
317 <213> ORGANISM: Artificial Sequence
319 <220> FEATURE:
320 <223> OTHER INFORMATION: Antisense Oligonucleotide
322 <400> SEQUENCE: 17
323 cagcagcatc tcgcccatgg                                    20
325 <210> SEQ ID NO: 18
326 <211> LENGTH: 20
327 <212> TYPE: DNA
328 <213> ORGANISM: Artificial Sequence
330 <220> FEATURE:
331 <223> OTHER INFORMATION: Antisense Oligonucleotide
```

VERIFICATION SUMMARY
PATENT APPLICATION: US/10/001,844

DATE: 12/11/2001
TIME: 20:33:04

Input Set : **A:\Pto.amc**
Output Set: **N:\CRF3\12112001\I001844.raw**

L:11 M:270 C: Current Application Number differs, Replaced Current Application No
L:11 M:271 C: Current Filing Date differs, Replaced Current Filing Date

OIPE

RAW SEQUENCE LISTING　　　　　　　　DATE: 12/11/2001
PATENT APPLICATION:　US/10/001,844　　TIME: 12:06:43

Input Set : **A:\isph-617_sequence.txt**
Output Set: **N:\CRF3\12112001\I001844.raw**

Does Not Comply
Corrected Diskette Needed

```
      4 <110> APPLICANT: C. Frank Bennett
      5        Lex M. Cowsert
      7 <120> TITLE OF INVENTION: ANTISENSE MODULATION OF SHH EXPRESSION
      9 <130> FILE REFERENCE: ISPH-0617
C--> 11 <140> CURRENT APPLICATION NUMBER: US/10/001,844
C--> 11 <141> CURRENT FILING DATE: 2001-11-16
     11 <160> NUMBER OF SEQ ID NOS: 49
     13 <170> SOFTWARE: FastSEQ for Windows Version 4.0
```

ERRORED SEQUENCES

```
    666 <210> SEQ ID NO: 49
    667 <211> LENGTH: 20
    668 <212> TYPE: DNA
    669 <213> ORGANISM: Artificial Sequence
    671 <220> FEATURE:
    672 <223> OTHER INFORMATION: Antisense Oligonucleotide
    674 <400> SEQUENCE: 49
    675 tcagctggac ttgaccgcca                                         20
E--> 678 1
E--> 681 1
```

VERIFICATION SUMMARY
PATENT APPLICATION: US/10/001,844

DATE: 12/11/2001
TIME: 12:06:44

Input Set : **A:\isph-617_sequence.txt**
Output Set: **N:\CRF3\12112001\I001844.raw**

L:11 M:270 C: Current Application Number differs, Replaced Current Application No
L:11 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:678 M:254 E: No. of Bases conflict, LENGTH:Input:1 Counted:20 SEQ:49
M:254 Repeated in SeqNo=49